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L14: Entry 1 of 4

File: PGPB

Aug 4, 2005

DOCUMENT-IDENTIFIER: US 20050169991 A1

TITLE: Sustained release torsemide dosage forms

Summary of Invention Paragraph:

[0075] A non-limiting list of suitable sustained-release materials which may be included in a sustained-release excipient according to the invention include hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials, waxes, shellac, sustained release polymers, and oils such as hydrogenated castor oil and hydrogenated vegetable oil. Certain sustained-release polymers include alkylcelluloses such as ethylcellulose, acrylic and methacrylic acid polymers and copolymers (such as Eudragit.RTM. by Rohm Pharma; and cellulose ethers, especially hydroxyalkylcelluloses (especially hydroxypropylmethylcellulose) and carboxyalkylcelluloses. Examples of acrylic and methacrylic acid polymers and copolymers include methyl methacrylate, methyl methacrylate copolymers, ethoxyethyl methacrylates, ethyl acrylate, trimethyl ammonioethyl methacrylate, cyanoethyl methacrylate, aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamine copolymer, poly(methyl methacrylate), poly(methacrylic acid) (anhydride), polymethacrylate, polyacrylamide, poly(methacrylic acid anhydride), and glycidyl methacrylate copolymers. Waxes include for example natural and synthetic waxes, fatty acids, fatty alcohols, and mixtures of the same (e.g., beeswax, camauba wax, stearic acid and stearyl alcohol). Examples of gums include, for example and without limitation, heteropolysaccharides such as xanthan gum(s), homopolysaccharides such as locust bean gum, galactans, mannans, vegetable gums such as alginates, gum karaya, pectin, agar, tragacanth, accacia, carrageenan, tragacanth, chitosan, agar, alginic acid, other polysaccharide gums (e.g. hydrocolloids), mixtures of any of the foregoing, and the like. Certain embodiments utilize mixtures of any of the foregoing sustained release materials in the sustained release excipient. However, any pharmaceutically acceptable hydrophobic or hydrophilic sustained-release material which is capable of imparting sustained-release of the active agent may be used in accordance with the present invention.

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delayed-release /de-layed-re-lease/ (-lad' re-les') releasing a drug at a time later than that immediately following its administration.

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L14: Entry 4 of 4

File: PGPB

Dec 11, 2003

DOCUMENT-IDENTIFIER: US 20030228361 A1

TITLE: Sustained release metoprolol formulations

Detail Description Paragraph:

[0067] A non-limiting list of suitable sustained-release materials which may be included in a sustained-release excipient according to the invention include hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials, waxes, shellac, and oils such as hydrogenated castor oil and hydrogenated vegetable oil. Certain sustained-release polymers include alkylcelluloses such as ethylcellulose, acrylic and methacrylic acid polymers and copolymers; and cellulose ethers, especially hydroxyalkylcelluloses (especially hydroxypropylmethylcellulose) and carboxyalkylcelluloses. Examples of acrylic and methacrylic acid polymers and copolymers include methyl methacrylate, methyl methacrylate copolymers, ethoxyethyl methacrylates, ethyl acrylate, trimethyl ammonioethyl methacrylate, cyanoethyl methacrylate, aminoalkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), methacrylic acid alkylamine copolymer, poly(methyl methacrylate), poly(methacrylic acid) (anhydride), polymethacrylate, polyacrylamide, poly(methacrylic acid anhydride), and glycidyl methacrylate copolymers. Preferred waxes include for example natural and synthetic waxes, fatty acids, fatty alcohols, and mixtures of the same (e.g., beeswax, cernauba wax, stearic acid and stearyl alcohol). Examples of gums include, for example and without limitation, heteropolysaccharides such as xanthan gum(s), homopolysaccharides such as locust bean gum, galactans, mannans, vegetable gums such as alginates, gum karaya, pectin, agar, tragacanth, accacia, carrageenan, tragacanth, chitosan, agar, alginic acid, other polysaccharide gums (e.g. hydrocolloids), mixtures of any of the foregoing, and the like. Certain embodiments utilize mixtures of any of the foregoing sustained release materials in the matrix. However, any pharmaceutically acceptable hydrophobic or hydrophilic sustained-release material which is capable of imparting sustained-release of the active agent may be used in accordance with the present invention.

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en·ter·ic (ĕn-tĕr'ĭk) also **en·ter·al** (ĕn'tĕr-əl)
adj.

Of, relating to, or being within the intestine.

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Thesaurus

Legend: [Synonyms] [Related Words] [Antonyms]

Adj. 1. enteric - of or relating to the enteron

enteral

2. enteric - of or relating to or inside the intestines; "intestinal disease"

intestinal, enteral

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E. coli	family Enterobacteriaceae
Empirin	genus Escherichia
enteric bacteria	klebsiella
enteric fever	phenyl salicylate
enterics	Pituitous

- References in classic literature

Here I rallied, and had already improved so far as to be able to walk about the wards, and even to bask a little upon the verandah, when I was struck down by **enteric** fever, that curse of our Indian possessions.

A Study In Scarlet by Doyle, Sir Arthur Conan

[View in context](#)

One night three troops of our squadron were ordered to a certain point whither they had patrolled the

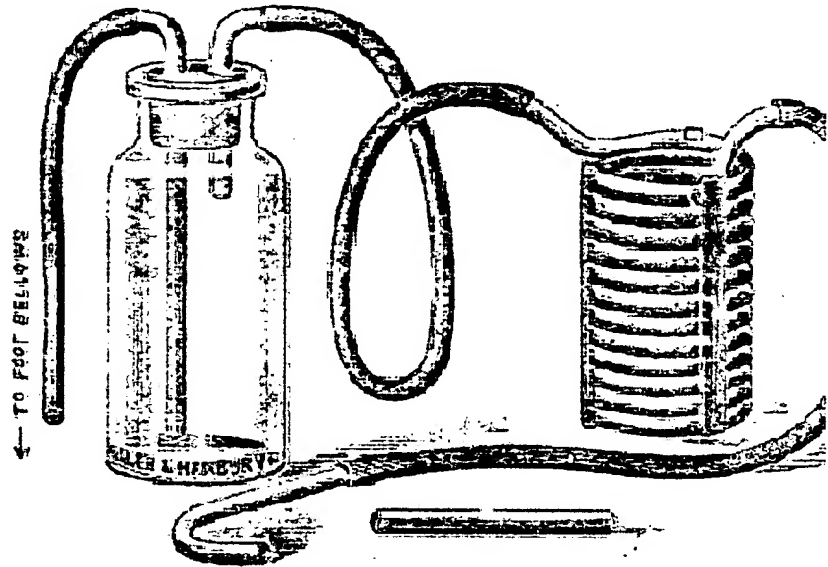
Local Anesthetic Use

Up

Dental Blocks

Intratesticular Blocks

Ring Blocks



1) AGENTS

a) Lidocaine

i) General

(1) Local anesthetic with quick onset and short duration of action

(a) Onset = 5 to 10 minutes

(b) Duration = 1 to 2 hours

ii) Dose

(1) Dogs

(a) 1.0 to 5 mg/kg (0.5 to 2.5 mg/lb)

(2) Cats

(a) 1.0 to 2.5 mg/kg (0.5 to 1.0 mg/lb)

iii) Precautions

(1) Potential CNS toxicity

(a) Usually manifests as seizure activity

iv) Cost

(1) Low

b) Mepivacaine

i) General

(1) Local anesthetic with quick onset and moderate

duration of action

(a) Onset = 5 to 10 minutes

(b) Duration = 2 to 3 hours

ii) Dose

(1) Dog

(a) 5 mg/kg (10 mg/lb) in dogs

(2) Cat

(a) 2.5 mg/kg (1.0 mg/lb)

iii) Precautions

(1) IV use is not currently recommended

iv) Cost

(1) Low

c) Bupivacaine

i) General

(1) Local anesthetic with slower onset and longer duration of action

(a) Onset = 20 to 30 minutes

(b) Duration = 3 to 5 hours

ii) Dose

(1) Dog and cat

(a) 1.0 to 2.0 mg/kg (0.5 to 1.0 mg/lb)

iii) Precautions

(1) Never give bupivacaine IV

(2) Potentially fatal cardiac toxicity

(a) Calculate doses carefully and aspirate carefully; guard against intravascular administration

(3) There is some debate about the use of intrapleural bupivacaine if a pericardiectomy has been performed due to the increased potential for cardiac toxicity

iv) Cost

(1) Moderate

2) APPLICATIONS

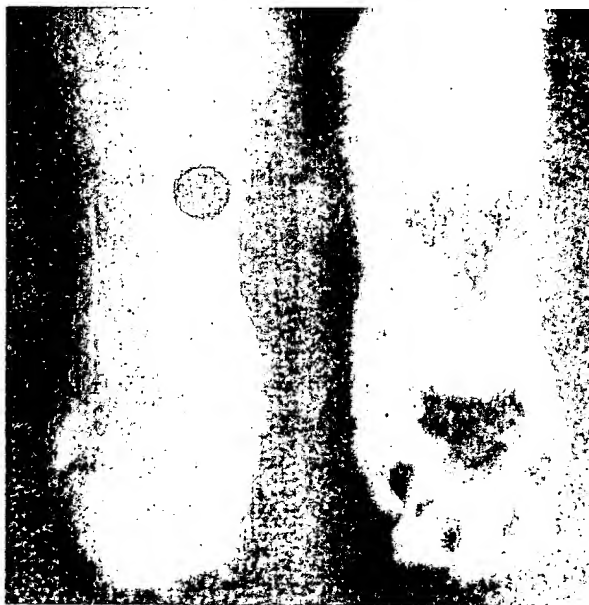
a) Consider adding an opioid to the local anesthetic

i) Both 0.075 mg/kg (0.035 mg/lb) morphine and 0.003 mg/kg (0.0015 mg/lb) buprenorphine have been shown to effectively double the analgesic duration when combined with lidocaine and bupivacaine^{1,2}

b) Outpatient/awake patient use

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- i) Mix 0.9 cc Lidocaine, 0.1 cc sodium bicarbonate, and cc of sterile water
 - (1) Reduced sting
 - (2) Volume is more important than concentration
- c) **Splash block**
 - i) Drip on or in SubQ space at closure of skin wound
 - ii) The effectiveness of splash blocks is in question
- d) **Ring blocks**
 - i) Mix 1.0 mg/kg (0.5 mg/lb) bupivacaine with 1.0 mg/lb (0.5 mg/lb) lidocaine and:
 - (1) Either 0.075 mg/kg (0.035 mg/lb) morphine or 0.0 mg/kg (0.0015 mg/lb) buprenorphine to effectively double the duration of analgesia ^{1,2}
 - (2) Sterile water q.s., if needed, to total 1 cc volume for cats less than 2.5 kg (5 lb).
 - (3) Sterile water q.s., if needed, to total 2 cc volume for cats 2.5 kg (5 lb) and over.
 - ii) Inject subcutaneously at the three sites demonstrated below:



- iii) You may drop the lidocaine if given prior to spay (give bupivacaine time to take effect)
- iv) Bupivacaine has significant potential to cause cardiac toxicity
 - (1) Calculate dose carefully
 - (2) Aspirate carefully before injecting
- v) **DO NOT USE EPINEPHRINE CONTAINING AGENTS**

vi) [Click here for an MS Excel Ring Block dose calculator](#)

e) Intratesticular blocks

- i) This is a very effective, low-cost application of local anesthetic agents
- ii) Mix 1.0 mg/kg (0.5 mg/lb) bupivacaine with 1.0 mg/l (0.5 mg/lb) lidocaine and:
 - (1) Either 0.075 mg/kg (0.035 mg/lb) morphine or 0.0 mg/kg (0.0015 mg/lb) buprenorphine to effectively double the duration of analgesia^{1,2}
- iii) Use a 25g 5/8" needle for most cats and a 22g 1 to 1 1/2" needle for dogs
- iv) Place the needle through the testicle starting from the caudal pole aiming for the spermatic cord
- v) It is OK, even desirable, for the needle to exit the testis proximally as it is the spermatic cord that will receive direct clamp stimulation
- vi) ASPIRATE BEFORE INJECTING
 - (1) Inject, expecting firm backpressure, while withdrawing the needle
 - (2) Expect to use about 1/3 to 1/2 of the drug volume per testicle leaving the organ firmly turgid
- vii) Repeat for other testicle
- viii) The left over drug can/should be used to place a derm incisional block
- ix) The total time for this procedure should be 1 to 2 min
- x) Drugs costs:
 - (1) 3 kg cat = \$0.04
 - (2) 55 kg dog = \$0.65
- xi) Videos

IT Block in 16 kg canine



Incisional block in 16 kg canine



Move mouse cursor over video window to play. Note aspiration before injection.

These are large files - be patient. If you have dial-up, forgetaboutit!

f) Intra-articular Injections

- i) Lidocaine

- (1) 2 mg/kg (1 mg/lb)
 - (a) With epinephrine prior to arthrotomy to help control hemorrhage
 - (b) Without epinephrine after joint closure
 - ii) Bupivacaine
 - (1) 1.0 mg/kg (0.5 mg/lb) after closure
 - iii) Generally, 4 - 6 ml fills a stifle
 - iv) Place in joint after closure or place lidocaine w/epinephrine in joint before arthrotomy, wait 5 minutes then proceed with surgery
- g) Mandibular Block**
- i) Palpate foramen digitally from oral cavity to guide needle
 - ii) Use 0.5 to 1.5 ml total volume
 - iii) Effective coverage includes:
 - (1) Lower teeth
 - (2) Skin and mucosa of lower lip
- h) Maxillary Block**
- i) 1.5 cm caudal to medial canthus
 - ii) Just ventral to zygomatic arch and ahead of the ramus
 - iii) Use 1.0 to 1.5 ml total volume
 - iv) Effective coverage includes:
 - (1) Maxilla and upper teeth
 - (2) Nose and upper lip
- i) Intercostal blocks**
- i) Block 2 spaces ahead and behind intercostal incision
 - ii) Place 0.25 to 1.0 ml per site along the caudal border of each rib near the level of the intervertebral foramen
 - (1) Do not exceed the dose guidelines above

¹ Buprenorphine added to the local anesthetic for axillary brachial plexus block prolongs postoperative analgesia. Candido KD, Winnie AP, Ghaleb AH, Fattori MW, Franco CD: Reg Anesth Pain Med. 2002 Mar-Apr;27(2):162-7

² The addition of opioids to local anaesthetics in brachial plexus block: the comparative effects of morphine, buprenorphine and sufentanil. Bazin JE, Mas C, Bruelle P, Fenies V, Groslier D, Schoeffler P: Anaesthesia. 1997 Sep;52(9):62

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Last modified: Thursday December 21, 2006.